Remarks

Claims 4, 8, 10, 12, 13, and 15 are pending in this application. Claim 3 is withdrawn from consideration as drawn to a non-elected species. Claims 1, 2, 5-7, and 14 have been canceled. Thus, claims 4, 8, 10, 12, 13, and 15 are under consideration. Claims 13, and 15 are amended herein to recite "cadaveric donor". Support for the use of cadaveric donor cells can be found at least on page 7, line 7; page 40, lines 7-9; and Examples 8 and 9 where the use of "cadaveric donors" is described. Claims 13 and 15 have also been amended to recite "a divalent anti-T cell diphtheria toxin binding site mutant immunotoxin directed at the CD3 epitope." Support for claims 13 and 15 as amended can be found at least in original claims 5-7 and throughout the specification. Support for the recitation of a "binding site mutant" can be found throughout the specification and at least on page 10, lines 9-10. No new matter is believed to be entered by these amendments. Additionally, Applicants believe that the amendments raise no new issues as the Examiner has already considered this limitation in the context of the priority claim.

Priority Claim

The Examiner has rejected Applicants' priority claim to U.S. Serial No. 09/636,251, now U.S. Patent No. 6,103,235 (the '235 patent) with respect to claims 13 and 15. The Examiner's reasoning with respect to these claims is that the application discloses pancreatic islet cell transplantation "only wherein the donor is a cadaver and only in a context wherein the immunotoxin is administered 0 to 6 hours before transplantation." Applicants respectfully submit that cadaveric donors are the primary, if not the only, source of pancreatic islet cells. Nevertheless, claim 13 and claim 15 have been amended to recite "cadaveric donor". Therefore, the issue of support with respect to the donor being a cadaver is now moot. Regarding the period of administration of the immunotoxin indicated by the Examiner, Applicants note that the Examiner has mistakenly removed this sentence from the larger context and in the process changed its meaning. Applicants note that column 9, lines 35-36, the specification specifically indicates that "the immunotoxin injection can also be made within a week or two prior to the

donor cell treatment." In this context, the '235 specification sets out examples of time-points during which the immunotoxin could be administered that fall within the one to two weeks prior to donor cell treatment. On column 9, lines 42-46, the specification sets out as one example that the administration of the immunotoxin could occur 0 to 6 hours prior to donor cells. This range is stated only as a preference and not as a limitation. Furthermore, the very next sentence states that "for practical reasons immunotoxin treatment and transplantation generally take place at about the same time (e.g., within 15 hours) because advance planning with cadaveric transplants is difficult." Column 9, lines 46-40 of the '235 patent. Clearly the Examiner's assertion that the disclosure is limited to 0 to 6 hours is incorrect, for the example provided in the next sentence falls outside the Examiner's asserted scope. At best, the example of immunotoxin treatment 0 to 6 hours prior to transplantation could be interpreted to be what Applicants felt was the best mode with respect to cadaveric cells at the time the '235 patent was filed. However, do to the presence of the statements that the treatment and transplantation could occur within 15 hours in the next sentence and within one to two weeks as stated earlier in the same paragraph, it is clear that the '235 patent discloses transplantation of the cadaveric cells (including pancreatic islet cells) from 0 hours to two weeks following treatment with the immunotoxin.

Applicants submit that claims 13 and amended claim 15 are fully supported by the '235 patent. Applicants note that support for the remaining limitations of claims in the '235 patent has been made of record in the previous response and was not challenged. However, for the convenience of the Examiner, Applicants have again provided support for the claims in the '235. Applicants note that support can be found for the recitation in claim 13 for "a method of inhibiting a rejection response of a pancreatic islet transplant" can be found at least on column 8, lines 10-18 of the '235 patent where inhibiting a rejection response is discussed and on column 9, lines 35-54 of the '235 patent where pancreatic islet cells as donor tissue for a transplant are discussed. Support for the recitation of "by inducing immune tolerance in the recipient" in claim 13 can be found at least on column 8, line 22 through column 9, line 3 of the '235 patent. Support for "comprising administering a divalent anti-CD3 diptheria toxin binding mutant immunotoxin," can be found at least on column 8, lines 10-18 and column 5, line 3 of the '235

patent, and support for "deoxyspergualin" can be found at least on column 8, lines 48-56 of the '235 patent where the use of immunosuppressants in conjunction with the immunotoxin is discussed. The '235 patent discusses time periods corresponding to the recitation of "during the peritransplant period," at least on column 9, lines 15-54. Additionally, the function of "reducing the number of T-cell lymphocytes" in claim 13 can be found at least on column 2, lines 44-49, column 8, lines 10-18, and column 9, lines 55-63 of the '235 patent, and "promoting long-term survival of the transplant" can be found at least in example 12 of the '235 patent, where the long-term survival of grafts using the claimed methods is discussed. Amended claim 15 finds support in the same places as claim 13. In light of the sited support, Applicants respectfully request reconsideration of Applicants' priority claim.

35 U.S.C. § 103

Claims 4, 8, 10, 12, 13, and 15 are rejected under 35 U.S.C. § 103 (a) as allegedly being obvious over U.S. Patent No. 6,103,235 (the '235 patent). Applicants respectfully traverse this rejection. Applicants previously submitted a corrected priority claim to U.S. Serial No. 09/636,251 which is a continuation of and claims priority to U.S. Serial No. 08/439,409, now U.S. Patent No. 6,103,235. The Examiner has denied this claim to priority. Applicants submit that claims 13 and amended claim 15 are supported by the priority documents as noted above. Applicants respectfully request reconsideration of the priority claim. In light of the support detailed above and favorable reconsideration, the present application claims priority to the '235 patent. Therefore, the present application and the '235 patent have the same priority date and the '235 patent cannot render obvious the present invention. Applicants submit that the present basis for rejection does not have merit, and its withdrawal is respectfully requested.

Claims 4, 8, 10,12, 13, and 15 are rejected under 35 U.S.C. § 103 (a) as allegedly being obvious over WO 96/32137 in view of Henretta et al. (*Transplantation Proceedings* (1994) 26: 1138-1139). Applicants respectfully traverse this rejection. Applicants have herein shown support for their claim to priority to U.S. Serial No. 08/843,409, now U.S. Patent No. 6,103,235 and requested reconsideration of the claim to priority. Thus, Applicants' have a priority date of

at least April 15, 1997. The publication date of WO96/32137 is October 17, 1996, less than one year prior to the April 15, 1997 priority date. The subject matter of the WO96/32137 publication represents the work of the Applicants. Applicants previously submitted a declaration of Dr. Neville under 37 C.F.R. 1.132 establishing the WO96/32137 represents the Applicants' own work. Thus the WO96/32137 publication is not prior art and cannot render obvious the present invention. In light of the declaration and applicants request for reconsideration of the priority claim, applicants believe this rejection has been overcome and respectfully request withdrawal of the rejection, as the remaining cited references fails to teach each element of the claimed invention

U.S.C. § 112, first paragraph

Claim 13 is rejected under 35 U.S.C. § 112, ¶ 1, for allegedly failing to have written support in the specification for the claim as amended. In particular, the Examiner has rejected claim 13 for allegedly lacking written description in the specification for "a divalent anti-CD3 diphtheria toxin binding mutant immunotoxin." The Examiner states that claims 5-7 (provided as Applicants' support for claim 13 as previously amended) "recite a divalent anti-T cell immunotoxin directed at the CD3 epitope, wherein the toxin moiety is a diphtheria toxin. Applicants note there is no scientific difference between an "anti-CD3 immunotoxin" and an "anti-T cell immunotoxin directed at the CD3 epitope" as CD3 is the T cell receptor and only present on T-cells. One of skill in the art would know that an anti-CD3 immunotoxin would have to be an anti-T cell immunotoxin. The important aspect to one of skill in the art would be that the immunotoxin targeted the CD3 epitope rather than CD4, CD8, or any of the myriad of other surface molecules on a T cell. Moreover, applicants note that support for an anti-CD3 immuntoxin can be found at least on page 4, lines 5-9; page 5, line 31; page 11, lines 15-16; page 18, lines 23-28; and elsewhere throughout the application. Thus, any amendment required by the Examiner to make such a change in the wording of claim 13 or any other claim is wholly unnecessary. Nonetheless, to further prosecution, Applicants have amended claim 13 to recite "a divalent anti-T cell diphtheria toxin binding site mutant immunotoxin directed at the CD3

epitope." Support for this amendment is noted above. Applicants note that that this amendment in no way limits the scope of the claim as the claim was clear and had support as previously written. Applicants believe this rejection has been overcome and respectfully request the rejection be withdrawn.

Claim 15 is rejected under 35 U.S.C. § 112, ¶ 1, for allegedly failing to have written support in the specification for the claim as amended. In particular, the Examiner has rejected claim 15 for allegedly lacking written description in the specification for the recitation of "a divalent anti-CD3 diphtheria toxin binding site mutant immunotoxin." Applicants have amended claim 15 to recite "a divalent anti-T cell diphtheria toxin binding site mutant immunotoxin directed at the CD3 epitope." Applicants note that support for this amendment can be found at least in original claims 5-7 as noted above. Applicants believe no new matter has been added by this amendment as the claim was clear as previously written.

The Examiner also contends that support is present only for "a method of pancreatic islet cell transplantation as a treatment for diabetes." However, as noted by the Examiner support in the disclosure for transplanting pancreatic islet cells can also be found on the last paragraph of page 8. Applicants note that the written description requirement only necessitates that description be present in the specification. 35 U.S.C. 112, first paragraph, does not require multiple descriptions. Thus, that applicants have support, even if just a single passage, is sufficient to meet the written description requirement of 35 U.S.C. 112. Moreover, Applicants note that original claim 13 also is not limited to methods of transplanting pancreatic islet cells for only treating diabetes. Claim 13 is based on a mechanism (transient T cell killing) that supports any transplant of pancreatic islet cells subject to T cell mediated rejection responses irrespective of the intended purpose of transplanting those cells. Therefore, the specification does provide support for methods of pancreatic islet cell transplantation including but not limited to treatment of diabetes as indicated by original claim 13 and on page 8 as noted by the Examiner. Applicants believe this rejection to be overcome and respectfully request the rejection be withdrawn.

Applicants note that claims 13 and 15 have also been amended herein to recite "cadaveric donor." As indicated above, support for these amendments can be found at least on page 7, line 7; page 40, lines 7-9, and Examples 8 and 9 where the use of "cadaveric donors" is described. Also, as noted above, Applicants believe that the amendments raise no new issues as the Examiner has already considered this limitation as evidenced by the Examiner's statement on page 2 of the October 14, 2005 Office Action indicating that the '235 patent discloses pancreatic islet cell transplantation "only wherein the donor is a cadaver.". Applicants believe this rejection to be overcome and respectfully request its withdrawal.

Pursuant to the above amendments and remarks, reconsideration and allowance of the pending application is believed to be warranted. The Examiner is invited and encouraged to directly contact the undersigned if such contact may enhance the efficient prosecution of this application to issue.

A Credit Card Payment Form PTO-2038 authorizing payment in the amount of $620.00, representing $500.00 for the Notice of Appeal fee for a large entity under 37 C.F.R. § 41.20(b)(1) and $120.00 for the Extension of Time fee for a large entity under 37 C.F.R. § 1.17(a)(1), a Notice of Appeal, and a Request for Extension of Time are enclosed. This amount is believed to be correct. However, should additional fees be required, the Commissioner is hereby authorized to charge any additional amount or credit any overpayment to Deposit Account No. 14-0629.

Respectfully submitted,

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CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.8

I hereby certify that this correspondence, including any items indicated as attached or included, is being deposited with the United States Postal Service as first class mail in an envelope addressed to: MAIL STOP AMENDMENT, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the date indicated below.

Gwendolyn D. Spratt — Date: 2-14-06